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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|--|-------------|----------------------|-------------------------|------------------|
| 09/516,061 | 03/01/2000 | Venkat Gopalan | 50093/016001 | 3858 |
| 21559 | 7590 | 12/24/2003 | EXAMINER | |
| CLARK & ELBING LLP 101 FEDERAL STREET BOSTON, MA 02110 | | | PATTERSON, CHARLES L JR | |
| | | ART UNIT | PAPER NUMBER | |
| | | 1652 | | |

DATE MAILED: 12/24/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

| | | |
|------------------------------|---------------------------|----------------|
| Office Action Summary | Application No. | Applicant(s) |
| | 09/516,061 | GOPALAN ET AL. |
| | Examiner | Art Unit |
| | Charles L. Patterson, Jr. | 1652 |

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM
 THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) Responsive to communication(s) filed on 06 October 2003.
- 2a) This action is FINAL. 2b) This action is non-final.
- 3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) Claim(s) 1,2,8-11 and 13-40 is/are pending in the application.
- 4a) Of the above claim(s) 22-28 and 30-40 is/are withdrawn from consideration.
- 5) Claim(s) _____ is/are allowed.
- 6) Claim(s) 1,2,8-11,13-21 and 29 is/are rejected.
- 7) Claim(s) _____ is/are objected to.
- 8) Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) The specification is objected to by the Examiner.
- 10) The drawing(s) filed on 06 October 2003 is/are: a) accepted or b) objected to by the Examiner.
 Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
 Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

- 12) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
 a) All b) Some * c) None of:
 1. Certified copies of the priority documents have been received.
 2. Certified copies of the priority documents have been received in Application No. _____.
 3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 13) Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.
 a) The translation of the foreign language provisional application has been received.
- 14) Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

- 1) Notice of References Cited (PTO-892) 4) Interview Summary (PTO-413) Paper No(s). _____.
 2) Notice of Draftsperson's Patent Drawing Review (PTO-948) 5) Notice of Informal Patent Application (PTO-152)
 3) Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____. 6) Other: _____

Art Unit: 1652

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 10/6/03 has been entered.

Claims 22-28 and 30-40 are withdrawn from further consideration as being drawn to non-elected species. The election as made in Paper No. 11. Applicants elected to prosecute SEQ ID NO:27 in Paper No. 11 and these claims attempt to add back claims to other sequences than that elected.

The disclosure is objected to because of the following informalities:

The recitation on line 21-25 of page 11 is objected to because it states that "[a]s shown in Fig. 2, the three dimensional structure reveals..." Figure 2 does not reveal anything concerning the three dimensional structure of the proteins but merely discloses the primary structure (sequence) of the amino acids and the nucleotides encoding it.

As stated previously, the broad black lines in Fig. 1 are objected to as they obliterate the residues under them. These are again present in the drawing filed 10/6/03. In addition, nearly all of the regions that were previously gray in what is now "Fig. 1 Continued" are now unreadable and are objected to. Perhaps applicant could make the print of the residue abbreviations white within the black regions.

Appropriate correction is required.

Art Unit: 1652

Claims 2, 16 and 20 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 2, 16 and 20 are confusing in that they recite sequences that were not elected for prosecution. Applicant urges that they not be limited to the elected species at this time because if generic claims are not allowed they will restrict the claims to the species elected. This statement is noted but the instant rejection is maintained until such time as generic claims are allowed or these claims are so limited.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 17 and 21 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. This rejection is repeated for the reasons given in the last action. Applicants arguments have been carefully considered but do not overcome the instant rejection.

Applicants argue in the Remarks and in the Gopalan declaration that "a skilled artisan can easily measure the enzymatic activity of an RNase P holo-enzyme of interest...using standard assays" and provide such a measurement in Exhibit 1. The fact remains that one of ordinary skill in the art would not know when they were infringing the instant claims as they are drawn to a polypeptide having "at least 20% of the enzymatic activity of an *E. coli* or *B.*

Art Unit: 1652

subtilis RNase P holoenzyme" and there is nothing taught about the enzymatic activity of these enzymes in the specification.

Claims 1, 2, 8-11, 13-21 and 29 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. After further reading of the specification and previous prosecution and discussions with other examiners, it was deemed that this rejection should be made. Claim 1 is not adequately described because it is claiming all bacterial RNase enzymes that are not some 59 RNase P enzymes listed in the claim. In order to adequately describe the instant claims, one would have to provide the sequences of all 59 of these excluded enzymes. Applicants have provided the sequences shown in Figure 1, which are some 44-52 amino acids of each enzyme. The entire enzymes are apparently 102-161 amino acids long. Also, the instant specification apparently teaches that if one analyzes a sequence with BLAST and then "at least 13 of the amino acids" of the twenty highly conserved residues shown in Figure 1 are identical, this polypeptide is "preferred" as being an RNase P enzyme and if a sequence "conserves at least nine of the...twenty amino acids if the *E. coli* RNase P protein sequence" this is "an RNase P consensus sequence". There needs to be some rule for determining which polypeptides are RNase P enzymes in the instant claims.

In addition, claim 1 requires that the polypeptides have RNase P enzyme activity and apparently it is not taught in the specification that any of the predicted polypeptides such as SEQ ID NO:20-38 have such activity. The pre-

Art Unit: 1652

umption is made that if they have similarity to known RNase P enzyme, they will also have activity, but this was apparently never tested.

Claims 1, 2, 8-11, 13-21 and 29 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The specification teaches that certain amino acid residues are "preferred" to occur in RNase P enzymes and that if 9 out of 20 identified amino acids are present, this is "an RNase P consensus sequence". However, as discussed *supra*, there is no rule in any of the claims as to exactly how many of the residues must be identical in order for the polypeptide to be RNase P, nor is there apparently any disclosure that SEQ ID NO:20-38 have RNase P activity.

Applicants argue that only routine experimentation would be required, cited *In re Wands* and other cites. They also present a declaration by Gopalan that shows that *N. gonorrhoeae* and *Porphyromonas gingivalis* RNase P have enzymatic activity and the Gopalan declaration states that there is only one RNase P in each bacterial species and the different accession numbers shown for some RNase P polypeptide sequences are due to multiple deposits of the same sequence. Such a statement by one of the inventors of the instant application with no further proof is not deemed to be probative. Some additional confirmation of this is required and without this confirmation it is maintained that there is more than one RNase P enzyme in at least some species. Also, it is not stated in the declaration that the *N. gonorrhoeae* and

Art Unit: 1652

Porphyromonas gingivalis RNase P enzymes assayed are the same as SEQ ID NO:27 and 31.

It is maintained that without some rule governing how to determine "an RNase P consensus sequence", undue experimentation would be required to practice the instant invention.

Claims 8-11, 13-14 and 18-21 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The instant claims are drawn to methods of identifying antibiotic agents by seeing if they interfere with the activity of an RNase P enzyme. While it is maintained that claim 8 defines what is considered "an antibiotic agent" within the claim itself, it is maintained that the specification does not teach one of ordinary skill in the art that such an agent is an antibiotic agent as is generally recognized in the prior art, i.e. that will inhibit the growth of a microorganism. Therefore it is maintained that the specification does not enable one of ordinary skill in the art to identify an antibiotic agent.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless -

- (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

Art Unit: 1652

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claim 1 is rejected under 35 U.S.C. 102(a or b) as being anticipated by either of Gress, et al. (AA), Guth, et al. (AB), Altman, et al. (AC & AD), Frank, et al. (AE), Gopalan, et al. (AF), Pace, et al. (AJ), Pascual, et al. (AK) or Peck-Miller, et al. (AG). This rejection is repeated for the reasons given in the last action. Applicants arguments have been carefully considered but do not overcome the instant rejection. Applicants argue that the Gopalan declaration states that there is only one RNase P in each bacterial species. It is maintained that, as discussion *supra*, such a statement by one of the inventors is not probative evidence alone. Therefore the instant rejection is maintained.

Claims 8, 10, 11, 13 and 14 are rejected under 35 U.S.C. 103(a) as being unpatentable over either of Potuschak, et al. (U), Mikkelsen, et al. (V) or Schroeder, et al. (W) in view of Spitzfaden, et al. (X). The primary reference have been characterized *supra*. The secondary reference teaches in the abstract and in the paragraph spanning pages 105-106 that inhibitors of RNase P may be used as antibiotics. It would have been obvious to use the RNase P enzymes taught in the primary references as an antibiotic, as taught in the secondary reference, absent unexpected results.

Art Unit: 1652

Claims 1, 2, 8-11, 13-21 and 29 are rejected under 35 U.S.C. 103(a) as being unpatentable over either of Spitzfaden, et al. (X), Gopalan, et al. (AF) or Thompson, et al. AO). The instant references teach that it is a normal and accepted practice in the area of molecular biology to align sequences according to some scheme such as the Clustal alignment scheme and to determine which residues are consensus residues. That is essentially what was done in the instant application. The instant claims do not contain any rule as to what residues are considered essential for an RNase P consensus sequence and, as discussed *supra*, there is not any indication of activity in SEQ ID NO:20-38. Therefore it is maintained that it would have been obvious to one of ordinary skill in the art to perform such a consensus alignment with known RNase P enzymes with at least a reasonable expectation of success in selecting active sequences.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Charles L. Patterson, Jr., PhD, whose telephone number is 703-308-1834. The examiner can normally be reached on Monday - Friday, 7:30-4:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapura Achutamurthy can be reached on 703-308-3804. The fax phone number is 703-308-4242.

Art Unit: 1652

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.



Charles L. Patterson, Jr.
Primary Examiner
Art Unit 1652

Patterson
December 15, 2003